“What Are the Consequences of In-Utero and Early Childhood Exposures to PCBs? A Review of Neurodevelopmental Outcomes Following PCB Exposure”

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Abstract Summary

✍ The relationship of pre and perinatal exposure to Polychlorinated Biphenyls (PCBs), and the subsequent effects on neurodevelopment remains a vexing question

✍ Research suggests many chlorine containing compounds, including PCBs, have a significant and negative effect on brain development

✍ Neurodevelopment encompasses a series of susceptible periods in which the brain is vulnerable to insult from toxins and toxicants

✍ Using the parameters of developmental period of exposure, this review investigates the neurodevelopmental effects of exposure to specific PCB congeners both pre and perinatally, while considering the effect of exposure to mixtures of PCBs with other toxicants. Additionally, the environmental and familial factors which are suspected in influencing cognitive development and performance will be investigated

Background

✍ Polychlorinated biphenyls (PCBs) are commercial mixtures which were used as coolants and lubricants in transformers, capacitors and other electrical equipment

✍ Due to health and environmental risks associated with PCB's, their manufacture, processing and distribution was banned in 1976; however they persist in the environment today

✍ Food consumption is the major source of body burden of PCBs in the general population, primarily through consumption of contaminated fish, meat, and dairy products

✍ Health indicators related to early PCB exposure include: neurodevelopmental changes, reduced birth weight, reproductive toxicity, cancer, disruptions to the endocrine system, liver, thyroid, dermal, ocular changes and auditory changes, and immunological alterations

✍ PCBs can be transferred from mother to developing fetus through the placenta

✍ Infants and young children consume a greater amount of food per kilogram of body weight; therefore they have a proportionately greater exposure to PCBs than do adults eating food with the same level of contamination

Method

✍ Literature search was conducted on PUBMED using the keywords: *polychlorinated biphenyls; neurotoxins; congeners; children’s neurodevelopment; rodent PCB studies; organochlorines; cognitive development; in-utero PCB exposure; perinatal PCB exposure; developmental exposure; gestation; neuropsychological testing; methyl mercury; dioxin-like; non dioxin-like; ortho substituted; Toxic Equivalency Factor; hazard identification; environmental tobacco smoke; parental education level; maternal age; body burden; breastfeeding; fish consumption; socioeconomic status.*

✍ Search was focused on, but not limited to, studies published from years 2000-2006

Conclusion and Future Direction

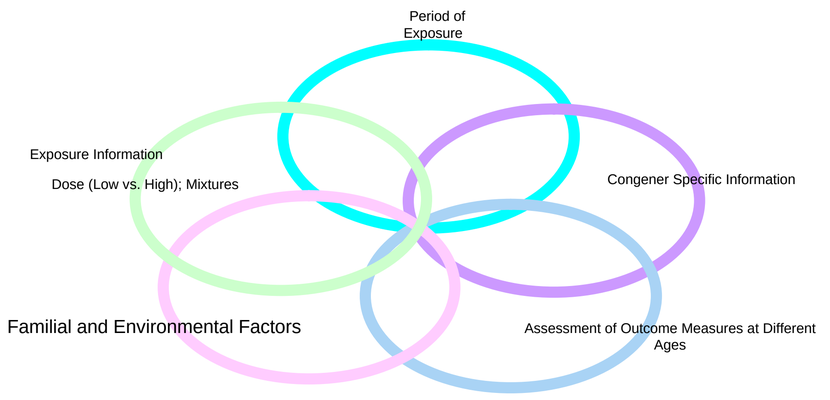
✍ The review of available literature suggests that a number of factors mediate the adverse effects seen with early developmental exposure to PCBs

✍ Neurodevelopment continues into adulthood and as such presents temporal challenges to the assessing uncertainty of adverse effects of developmental exposure to PCBs.

✍ In order to assess the ontogeny of function the use age-appropriate domain specific assessment measures are necessary to obtain the most detailed information on functional impairment. The review of the literature provides some consistency in effects on specific functional domains (e.g., cognitive, motor development auditory impairments).

✍ Currently, some studies provide lipid adjusted does metrics, while some do not. Future studies should provide lipid adjusted measures for total PCBs; however, separate lipid adjusted measures for specific congeners are necessary to understand specific hypothesized modes of action.

✍It would be ideal to conduct a longitudinal study which would assess function at multiple developmental stages and lipid adjusted exposures measures at several developmental stages. This would provide information on persistence of an adverse outcome as well as possibly latency of an effect.



Human Prenatal Exposure

	N	Biomarker of exposure	Congener*	Age Assessment	Domain affected	Outcome Measure	Confounders	Author/Group
	435	Cord blood; umbilical cord; questionnaire for diet	138, 153, 180	7 years	lexical development; attention; anterograde memory, effect seen with MeHg exposure – possible latent with PCB	Finger tapping; hand-eye coordination.; Boston naming test; continuous performance. test; Wechsler Intelligence Scale for Children; California verbal learning test; Neuropsych. and sensory testing	Seafood exposure; confound. with cord blood mercury	Grandjean 2001 Faroe Islands
	212	Cord blood; milk; Maternal Hair	Highly chlorinated PCBs	38 and 54 months	Significant at 38 months; no relationship at 54 months	McCarthy Scales of Children's Ability	SES; maternal IQ; ma ed; home env; cig smoke – interaction of PCBs and MeHg	Stewart 2003 Oswego
	1259	Ma serum during pregnancy, delivery and post partum	28, 52, 74,105, 118, 138, 153,170, 180,194, 203	8 months	No effect	Bayley Scales of Infant Development	**most non-breastfeeding (15%)**adjusted for ma education , birth order	Daniels 2003 Collaborative perinatal Project
	810	Maternal blood serum from 3rd trimester	28,52,74, 105,118, 138,53, 170,180, 194,203	8 years	No association between background levels of PCBs and auditory deficits	Audiometric evaluation	Adjusted for race sex	Longnecker 2004 collaborative perinatal project
	202	Umbilical. Cord blood; maternal hair	Not indicated	8 and 9 ½ years	Impaired response inhibition	Continuous Performance Task at age 8 and extended version at 9 ½	Maternal IQ ; MeHg and lead	Stewart 2005 Oswego
	894	Maternal serum during pregnancy and post partum	74;105; 118;138; 153;170; 180	7 years	No effect – in utero exposure to background levels of PCBs were not associated with lower IQ at age 7	Wechsler Intelligence Scale for Children	Old sample; no breastfeeding; low education; smokers; looked at background levels of PCBs	Gray 2005 collaborative project
	212	Cord blood; maternal blood; breast milk Child: Blood and hair samples		11 years	Lower full scale and verbal IQ scores	Scales of Infant Development; Wide Range Achievement Test; Woodcock- Johnson	SES contr. DDT Lead Methylmercury	Jacobson 2005 Michigan
	150	Ma serum during third trimester	15,28,56, 66, 74, 82,99, 101,105, 118,138, 146,153, 156,167, 170,174, 177,178, 180,183, 187,199, 203	4 yrs; 7 yrs for neurological soft signs 17 years for psych. And height and weight measures	Ortho subs. PCBs reduced weight through 17 y among girls not boys – tri ortho sub marginally assoc. with increased height in boys	Height and weight measurements	Neurological soft signs already present at 7 years; ma ed, SES, height, weight breastfeeding; maternal smoke; maternal age; 73% boys	Lamb 2005 NYC

Human Perinatal Exposure

	N	Biomarker of Exposure	Congener	Age Assessment	Domain affected	Outcome Measure	Potential Confounders	Author/Group
	171 mother/infant pairs	Cord blood, breast milk	138, 153, 180	7, 18, 30 and 42 months	Decreased mental and motor development to 42 months of age	Bayley Scales of Infant Development; Kaufman Assessment Battery; HOME	ETOH and smoking; APGAR; duration of breastfeeding; parent education; maternal IQ	Walkowiak 2001 Germany
	337	Child blood serum	101,118,138, 153;170,180, 183,187	7 years	Higher OC concentrations with increased duration of breastfeeding	Questionnaires (living condition; info from mother, father and child) Child height and weight	Breastfeeding, parity, smoking; DDE, HCB, HCH	Karmaus 2001 Germany
	207	Maternal and cord plasma; breast milk	118, 138, 153, 180	7.5 years	Differences in play behavior	Preschool Activity Inventory; HOME; Wechsler (parent IQ)	Dioxins; parental IQ and education	Vreugdenhil 2002 Netherlands
	102 mother/infant pairs	Cord serum	28,52,101, 118,138,153 and 180	13 months (± 6 wks)	Marginally decreased psychomotor development	Bayley Scales of Infant dev. and Griffiths Mental Dev Scales	SES, maternal IQ, ETOH, smoking, parity, breastfeeding duration	Ribos-Fito 2003 Spain

Animal Prenatal Exposure

	Species	Congener	Age exposed/ Assessment	Domain affected	Areas Assessed; Outcome Measure	Author/Group
	Rat	118	Pg rats exposed single dose 375 ug/kg of pcb 118 on GD 6	Decrease in thyroxine and TSH levels	Thyroid hormone status	Kuriyama 2004
	Rat	Aroclor 1254; 4-OH-CB 107	Exposed GD 10-16 with 25 mg/kg PCB;	habituation; decrease thyroxine; auditory thresholds neurotrans. levels	Open field paradigm; passive avoidance experiments; thyroid hormone status; catalepsy	Meerts 2004

Animal Perinatal Exposure

	Species	Congener	Age exposed/ Assessment	Domain affected	Areas Assessed; Outcome Measure	Author/Group
	Rat	1254	PND 60 (adult rat)	Decreased weight and motor activity (30 mg/kg); altered neurotransmitter levels	Motor activity; neurochemical disruption (thyroid hormone)	Kodavanti 1998
	Rat	1254	E: GD 6- PND 21 A: PND 17, 28, 43, 65	Subtle neurobehavioral effect	Functional Observation Battery (FOB) and Assessment of Motor Activity	Bushnell 2002
	Rat	1254	E: 4 weeks prior to breeding – PND 16 A:PND 60	Additive effect with Mehg + PCB = impaired. rotating rod	Motor testing; rope climb; Parallel bars; rotating rod	Roegge 2004
	Rat	35%1242; 35% 1248; 15% 1254; 15% 1260	E: 28 before mating to PND 21 A: 200 days old	Auditory impairment	Distortion Product Otoacoustic Emissions (DPOAE) testing and Auditory Brainstem Response (ABR)	Powers 2006

*Congeners in red are dioxin-like

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